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What's New in Thyroid Surgery

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ALTHOUGH relatively little new data have been developed during the past several years regarding the etiology of hyperthyroidism, enormous strides have been made in the treatment of the disease. In spite of the great progress made in methods of treatment, controversy still exists as to the preference for types of treatment. Three major types of therapy—(1) subtotal thyroidectomy, (2) anti-thyroid drugs, and (3) radioactive iodine—are being utilized today. Since favorable results are reported with all three of these different forms of treatment, it is obvious that it will require several more years' study before decision as to which is the best can be reached. However, there is already enough information about all three to suggest that one method of treatment may be superior in a certain group of patients and one of the others superior in another group. It is very probable that the greatest problem in this field during the next few years is going to be to decide the boundary lines of groups of patients in whom one method is better than another.

DIAGNOSIS OF HYPERTHYROIDISM

The diagnosis of hyperthyroidism is really outside the limits of this presentation. However, since differential diagnosis is so important in deciding whether or not specific therapy is necessary, it may be well to comment on two or three important points in differential diagnosis of the doubtful cases. In the first place, administration of Lugol's solution over a period of several days is of extreme value in establishing the diagnosis in doubtful cases, insofar as the drug produces a sharp improvement in symptoms within six to ten days if the manifestations are

produced by hyperthyroidism. During the past two or three years it has been shown by several workers that the administration of radioactive iodine may be very helpful in establishing a diagnosis, but unfortunately there is a great variation in methods reported. In the method reported by Werner and associates¹⁰ a dose between 40 and 100 microcuries is given to the patient and radioactivity in the thyroid measured with a Geiger counter, placed at a standard distance of 15 cm. from the neck, with the isthmus of the thyroid identified as the center of the field. The measurements are taken at the end of 24 hours. These investigators studied 57 patients with euthyroidism. The radioiodine uptake by the thyroid at the end of 24 hours ranged between 7 and 49 per cent of the tracer dose given. In this group 91 per cent of the patients had thyroid uptake below 35 per cent. The same investigators studied uptake in 97 patients with hyperthyroidism. In 94 per cent of this group the uptake exceeded 35 per cent. It is very significant that in a series of 21 patients studied following thyroidectomy with good results and return of basal metabolic rate to normal, 38 per cent showed uptake above 35 per cent. In 44 patients with nontoxic diffuse or nodular goiter, the uptake was the same as in the normal individuals. In acute thyroiditis the uptake was low, but in chronic thyroiditis it was low in only one of the 17 patients in whom the test was performed. In carcinoma of the thyroid the uptake was normal in the nine patients studied.

Studies on the amount of protein-bound iodine following ingestion of radioactive iodine for diagnostic study will add to the accuracy of the test. For example, 24 hours after ingestion of radioactive iodine, McConahey and associates⁶ found that 75 per cent or more of the iodine was present in the protein-bound form in hyperthyroid patients. In euthyroid persons, the iodine 24 hours after ingestion was found in the protein-bound form in quan-

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tities less than 45 per cent. In one patient with myxedema, the amount of protein-bound iodine found 24 hours after ingestion of radioiodine was too small to be measured.

TREATMENT BY THYROIDECTOMY

Cattell² of Boston has adequately summarized the results with subtotal thyroidectomy. In reporting on a study of 1,630 patients observed between 1943 and 1949 at Lahey Clinic, he noted that relief of symptoms was obtained permanently in 90 to 95 per cent of patients. The operative mortality rate in this group of patients was 0.24 per cent. In a closer analysis of the first 1,000 consecutive patients in this series, he noted that postoperative complications were encountered with an incidence indicated in Table 1.

TABLE 1.—*Surgical Treatment of Hyperthyroidism*
SUMMARY—1,000 CONSECUTIVE PATIENTS
(After Cattell, in Tr. Amer. Goiter Assn., 1949)

	Per cent
Hemorrhage	2.7
Tracheotomy	1.3
Postoperative hypothyroidism	4.5
	8.5
Tetany	1.5
Nerve injury	1.0
Recurrence	2.4
Mortality	0.2
	5.1

In the series reported by Cattell, all patients were prepared preoperatively with one of the antithyroid drugs, most recently propylthiouracil.

There is not total agreement regarding the use of these drugs supplementing surgical therapy. However, it is the author's opinion that preparation of patients with propylthiouracil before thyroidectomy will result in a much lower mortality rate. It is his custom to treat all patients with hyperthyroidism with propylthiouracil. As will be discussed later, a small number of this group, including those with small glands, symptoms of recent origin, and those with mild toxicity, have been treated for a long period of time in the hope that permanent remission might be obtained with medical treatment. Propylthiouracil is given until the patient's basal metabolic rate approaches normal. In that group in which resort to thyroidectomy has been decided upon, Lugol's solution is then started. After 12 to 15 days of treatment with Lugol's solution, the propylthiouracil is discontinued. Four to six days later operation is performed.

All surgeons agree that treatment with antithyroid drugs increases vascularity of the gland, although this increase in vascularity is disturbing to the surgeon in only a small percentage of cases. Preliminary ligation of the inferior thyroid artery (i.e., at the time of operation), as practiced by many surgeons, will prevent significant bleeding. In the author's

opinion, utilization of propylthiouracil in preparation of patients for thyroidectomy will lower the mortality rate following operation. Because of the low mortality rate following thyroidectomy, it will take a very large series of cases to prove this point. In over 1,000 patients having thyroidectomy during the ten-year period between 1936 and 1946 at Illinois Research Hospital, the mortality rate was slightly less than 1 per cent. However, during the past three to four years when antithyroid drugs have been used in preparing patients for thyroidectomy there have been no postoperative fatalities in perhaps 300 thyroidectomies.

TREATMENT WITH ANTITHYROID DRUGS

In an attempt to obtain thorough evaluation of the antithyroid drugs, Astwood¹ has adopted the principle of using this method to the exclusion of others. Although propylthiouracil is the drug of choice, Astwood reports fairly effective results following the use of methylthiouracil and mercaptimidiazole. During the past few months the present author in association with Fowler and Heidenreich has used another drug, iodothiouracil, in about 25 patients. Utilizing the dose of 150 mg. daily, as originally suggested for this drug, satisfactory results in reduction of hyperthyroidism were obtained in no more than 50 per cent of patients. However, with twice or thrice that dose fairly effective results have been obtained, although as yet no advantage of this drug over propylthiouracil has come to light. It was thought originally that this drug might have a more rapid effect than the other antithyroid drugs.

In an analysis of 300 patients given propylthiouracil over a four-year period, Astwood noted that with the dosage of 150 mg. a day about 20 per cent of patients did not respond properly. However, when this dose was increased to 300 mg. a day, response was satisfactory in all but 4 per cent. The present author, as well as others, has had the same experience, namely that with proper dosage of propylthiouracil very few patients will fail to be relieved of hyperthyroidism. As to patients treated with propylthiouracil as a major form of treatment, Astwood reports that detailed data are available on 137 who were treated for a prolonged period of time. Of this group 62 per cent obtained permanent remission, which at the time of his report was of six months' to three years' duration. If the patient is going to have a recurrence of hyperthyroidism following cessation of the drug therapy, symptoms usually will be shown within two months. With the increasing passage of time beyond this period with freedom from symptoms, there is a decreased incidence of relapses. However, patients may be free from symptoms for as long as two to three years and then have recurrence of symptoms.

At Illinois Research Hospital a small group of patients with symptoms of short duration or with small glands or with mild symptoms of antithyroid therapy alone was studied. These patients were treated for six to eight months with the drug before therapy was stopped, and 35 to 40 per cent of them

had remission. However, this represents a picked group of patients and these figures cannot be looked upon as an index of the effect of the drug in all patients with hyperthyroidism.

TREATMENT WITH RADIOIODINE

Soley⁸ in an article published in 1949 analyzed results of the use of radioactive iodine in 288 patients with hyperthyroidism in numerous clinics throughout the country. One of the greatest difficulties in the use of radioactive iodine is in the inability to establish a given dose for the patient. It is well known that in general the amount of iodine required is related to the weight of the gland. After experimenting with doses of various sizes, most workers have found that a dose of 100 micrograms of radioiodine per gram of thyroid tissue will eliminate hyperthyroidism in the majority of patients. However, Soley reported that the reaction was quite inconsistent in that some patients were relieved of symptoms with as little as 23 micrograms of radioiodine per gram of thyroid tissue, whereas others required as much as 575 micrograms. In the series analyzed, at least two patients became myxedematous with less than 50 micrograms per gram of thyroid tissue.

In the series of cases analyzed by Soley, the estimated average weight of the thyroid before treatment was 43 gm. After treatment, the weight of the thyroid was estimated at 20 gm. The average time required for the return of the basal metabolic rate to normal was slightly less than five months. A major complication was postoperative hypothyroidism or frank myxedema, which occurred in 8.5 per cent of patients.

In the 288 patients treated with radioiodine there were five deaths, which is approximately the same mortality rate as occurs in subtotal thyroidectomy. It might be said that it is unfair to attribute deaths in this series to the therapy, since two of these patients died of myocardial infarction, two died of vascular accidents of the brain and one died of cardiac failure. It might likewise be stated that at present practically all postoperative deaths following thyroidectomy are of the same type, namely cardiac or apoplectic. Accordingly the mortality rate largely relates to the normal death rate occurring over the period when therapy is being undertaken. Under such circumstances the figures would be unfair to treatment with radioiodine, since the patients being treated are observed over a period of four to six months, whereas patients after operation are held in the hospital no longer than six to ten days.

Of the 288 cases studied by Soley, results were good in 83 per cent and fair in 9.7 per cent. In 5.5 per cent, failure was reported.

Werner and associates¹⁰ also noted that the initial dose of radioiodine is adequate in only about two-thirds of patients. They called attention to the fear expressed by many investigators that carcinoma might develop in these glands years later. The basis for this fear is related to the fact that radio-autography shows an irregular collection of iodine in the

glands. If iodine is concentrated in certain areas of the gland, it is conceivable that damage leading to anaplastic changes might take place. It would appear that 15 or 20 years might be required for this transformation. Accordingly, many workers have reserved treatment with radioiodine for patients in the older age groups.

The treatment with radioiodine might be summarized by saying that the drug is effective alone in hyperthyroidism, but that the dose required is inconsistent. Because of the slight danger of production of anaplastic changes years after therapy, it would presumably be desirable, for the present, to confine use of the drug to people in the later decades of life. There appears to be strong indication for its use in recurrent hyperthyroidism following thyroidectomy since the drug will be effective in 90 per cent of such cases, whereas a second operation is effective in little more than 50 per cent of patients with recurrence. Patients with parathyroid deficiency or recurrent laryngeal nerve damage would likewise be good candidates for radioiodine therapy rather than operation. Opinions differ as to the preference in elderly people with cardiac failure. In general, toxic nodular goiter should not be treated with radioiodine except in the circumstances previously mentioned.

CARCINOMA OF THE THYROID

There is considerable difference of opinion as to the incidence of carcinoma of the thyroid, largely because of the difficulty in making a diagnosis from the microscopic slide and because of the great variation in the degree of malignancy. There is no doubt that several years ago the diagnosis of carcinoma was made too often. It is barely possible that the extreme caution in diagnosis urged by pathologists throughout the country during the past few years has swung the pendulum to the other side, and that now the diagnosis is not made often enough. For example, a patient recently admitted to the Illinois Research Hospital had had thyroidectomy 20 years previously, with a diagnosis of nontoxic nodular goiter. There was a nodule in the anterior portion of the neck which, upon histologic examination, turned out to be carcinoma of the thyroid. Further exploration revealed metastatic nodules in the left side of the neck occupying the region from which the thyroid lobe had been removed. There was actually no remnant of the thyroid lobe left on this side, indicating that the tumor could not have been a new tumor of recent origin. This prolonged survival is not unique; investigators have observed many patients for years with metastases changing very little over the course of several years.

The controversy regarding the exact origin of aberrant goiter has been crystallized considerably during the last few years. It is now fairly well agreed that aberrant thyroid nodules are in reality metastatic lymph nodes. It has been shown by many workers that if the ipsilateral thyroid lobe is removed and examined carefully by serial section, the primary lesion can be found with practically no ex-

ceptions. The degree of malignancy in aberrant goiter is actually less pronounced than in the usual type of carcinoma of the thyroid, as has been emphasized by Ward⁹ and others.

As has already been indicated, considerable difference of opinion exists relative to the incidence of carcinoma of the thyroid. In some studies conducted at the Illinois Research Hospital six years ago, Cole and associates³ noted that carcinoma was present in 17.1 per cent of their patients having thyroidectomy for nontoxic nodular goiter. This figure appeared remarkably high, but this was perhaps the first time that the incidence of carcinoma was studied in relation to the various types of goiter. In that series the percentage of carcinoma in toxic nodular goiter was only 1.2 per cent, and in toxic diffuse goiter it was only 0.2 per cent. Since that series was small, the author again reviewed his case records in 1948, but found approximately the same incidence (namely 17.2 per cent) of carcinoma in nontoxic nodular goiter (see Table 2).

Table 3 illustrates the incidence of carcinoma in various types of goiter, as obtained from reports in the literature. In addition to the figures shown in Table 3, Cope and associates have reported an incidence of 10 per cent carcinoma in all nodular goiter, and 19 per cent in goiters consisting of single nodules. Accordingly, it appears that when detailed studies are made of a large series of patients operated upon for goiter, a high incidence of carcinoma is found in patients with nontoxic nodular goiter. It is appreciated by all workers that nontoxic nodular goiter in children is associated with perhaps a still higher incidence of carcinoma, varying between 20 and 40 per cent in different localities.

It is perhaps true that carcinoma of the thyroid is, to some extent, a geographic disease insofar as

goiter itself is a geographic disease. The exact role of geography is not fully understood in the incidence of carcinoma.

TREATMENT OF CARCINOMA

Although controversy likewise exists as to the treatment of carcinoma, during the past few years certain points have crystallized from the mass of indeterminate data. Some of the difficulty in arriving at an opinion as to the best form of treatment lies in the fact that so many different types of therapy are available and are being used. For example, carcinoma of the thyroid is being treated by (1) subtotal thyroidectomy, (2) total thyroidectomy, (3) radical resection of the neck, (4) x-ray therapy, (5) radium therapy (radon seeds), and (6) radioactive iodine. Most workers will agree that the tumor should be removed if possible, largely because it has now been demonstrated that carcinoma of the thyroid will take up significant quantities of radioactive iodine in only about 10 per cent of cases. The treatment of metastatic carcinoma of the thyroid with radioactive iodine has been discouraging but has received renewed support by Rawson and associates,⁷ who discovered that total destruction of the thyroid increases the uptake of radioactive iodine by the metastatic nodules. For example, in eight of 13 cases of adenocarcinoma, the tumor assumed the capacity to concentrate radioactive iodine after the thyroid was removed. The time required for these changes to take place varied between one and 32 months. In one case in which the patient had a solid adenocarcinoma, a metastatic tumor which did not take up iodine even after development of myxedema, was found to concentrate iodine after the patient was given thyroid-stimulating hormone (Armour's thyrotropic hormone). In four

TABLE 2.—Incidence of Carcinoma in Nodular Goiter (Including Toxic, Nontoxic and Carcinoma) at the Illinois Research Hospital 1936-1948

(After Cole and Associates, Tr. Amer. Goiter Assoc., 1949)

Type of goiter	1936-1944		1944-1948		1936-1948	
	No. of Cases	% Carcinoma	No. of Cases	% Carcinoma	No. of Cases	% Carcinoma
Toxic nodular	330	1.2	48	0	378	1.0
Solitary	(71)	0.0	(17)	0	(88)	0.0
Multinodular	(259)	1.6	(31)	0	(290)	1.4
Nontoxic nodular.....	192	17.1	93	17.2	285	17.15
Solitary	(92)	(24.0)	(51)	(25.5)	(143)	(24.4)
Multinodular	(100)	(11.0)	(42)	(7.1)	(142)	(9.8)
Total.....	522	7.2	141	11.3	663	8.0

TABLE 3.—Incidence of Carcinoma in Nodular Goiter as Obtained from Numerous Reports in the Literature

(After Cole and Associates, Tr. Amer. Goiter Assoc., 1949)

Author	No. of Patients with Nod. Goiter (Toxic and Nontoxic)	Per Cent Carcinoma in Nod. Goiter (Toxic and Nontoxic)	No. of Patients with Nod. Nontoxic Goiter	Per Cent Carcinoma in Nod. Nontoxic Goiter	Per Cent Carcinoma in Solitary Nontoxic Nodular Goiter
Brenzier & McKnight (6); Charlotte, N. C., 1940.....	2,324	4
Horn & Assoc. (7); Philadelphia, Pa., 1947.....	1,135	6.3	637	9.8
Crile: Cleveland, Ohio, 1948.....	537	5.6	274	10.9	24.5
Ward: San Francisco, 1947.....	3,539	4.8	15.6
Cole & Assoc.: Chicago, Ill., 1948.....	663	8.0	285	17.1	24.4

patients with papillary adenocarcinoma, Rawson and associates found no increase in concentration of iodine in the metastatic lesions after removal or destruction of the thyroid lobe. However, since surgical removal or destruction of the thyroid with radioactive iodine is fairly effective in increasing the uptake of iodine by the metastatic nodules in a large percentage of patients, it appears that this procedure should be resorted to in every operable case. The only point of indecision will lie in whether the remaining thyroid should be removed surgically or destroyed with radioactive iodine. At present there is no consensus on that point although there might be some advantages to surgical removal.

As stated previously, there is a difference of opinion regarding the type of operation to be performed for carcinoma of the thyroid although most workers will agree that the tumor should be removed if possible and perhaps treatment given later with radioactive iodine and/or x-ray therapy. Some surgeons are of the opinion that if the tumor is small and located deep within the body of the thyroid lobe, subtotal thyroidectomy may be sufficient. However, as more experience accumulates with carcinoma of the thyroid, the author is inclined to be more and more radical. For example, during a subtotal thyroidectomy eight years ago, a small tumor was found deep in the body of one lobe. After considerable debate at the time, it was decided not to remove the entire lobe, although the amount of tissue left in place was no more than 3 gm. on the posterior capsule. However, a few months ago the patient returned with a large recurrence in the remnant of the thyroid and numerous metastatic nodules including invasion into the jugular vein. Of course it must be admitted that this recurrence might have taken place even though a total thyroidectomy on that side with a radical excision had been done. The case of another patient, previously referred to in this presentation, may illustrate the advisability of radical resection. Thyroidectomy had been done 20 years previously and on admission to the Illinois Research Hospital a few months ago the patient had a mass in the anterior portion of the neck which proved to be carcinoma. Further exploration revealed several metastatic nodules in the left side of the neck, but no remnant of thyroid tissue. It is apparent that 20 years ago the surgeon removed the right lobe completely. Again, it cannot be said whether or not radical resection would have cured this patient. However, since radical resection for carcinoma of other organs has been accepted without question, it would appear to the author that the same philosophy should be applied in carcinoma of the thyroid gland.

Perhaps this preference for radical therapy has been influenced by the fact that of 16 patients with carcinoma of the thyroid observed by the author during the past four years, 11 are already dead. It should be stated, however, that in about one-half of the 16 cases the lesions were inoperable when the patients were first observed.

THYROIDITIS

Acute thyroiditis. The need for surgical treatment of this condition is dependent upon the causative factor, as indicated by whether suppuration does or does not develop. In practically all cases in which there is suppuration the disease is pyogenic (streptococcus or staphylococcus, more commonly the former). In the author's opinion, at least some of the cases not proceeding to suppuration are viral in origin. This statement is based on the fact that a large percentage of patients with acute nonsuppurative thyroiditis give a history of having had upper respiratory infection a few days before thyroiditis developed; it is fairly well agreed that many of these respiratory infections are viral in origin. Nonsuppurative thyroiditis runs its course within a few weeks and, with the exception of a few of the more severe cases, all symptoms subside within that time. In general, no therapy has been of significant value in such cases, although some clinicians have gained the impression that thiouracil compounds hasten recovery. Certainly operation is not indicated. On the other hand, surgical incision of the fluctuant area is indicated in treatment of suppurative thyroiditis.

Chronic thyroiditis (Hashimoto's disease and Riedel's disease.) The cause of these two lesions is still more obscure than that of acute thyroiditis. However, a fair amount of evidence is available to the effect that infection is not the cause in either of the two. One point is fairly certain, namely, that acute thyroiditis is not followed by chronic thyroiditis of the types just referred to. A few workers have suggested that Hashimoto's disease is an early stage of Riedel's disease, but during the last two or three years there has appeared to be a growing conviction that the two lesions do not represent stages in the same process, but are two separate entities. The fact that Hashimoto's disease is always bilateral and Riedel's disease commonly unilateral supports the idea that the former cannot be the precursor of the latter.

Hashimoto's disease. Although it is fairly well agreed that thyroidectomy should be done in treating this disease, there is no agreement as to how much thyroid should be removed. This indecision is accentuated somewhat by the fact that at times the disease is accompanied by mild hyperthyroidism at the onset. Unfortunately the diagnosis of Hashimoto's disease can rarely be made clinically. Often, indeed, the diagnosis is not made until the tissue is examined microscopically. Davison and Letton⁵ noted that following total thyroidectomy mild myxedema developed in 61.5 per cent of 28 patients observed by them. Hypothyroidism occurred in 89 per cent of the total number of cases. Obviously, total thyroidectomy should give rise to a high incidence of hypothyroidism. Some workers believe that Hashimoto's disease is best treated by x-ray therapy, particularly since the incidence of hypothyroidism will be lower with this treatment than after total thyroidectomy. It is barely possible that if a way to select the patients were known, thyroidectomy

might not be necessary in a certain percentage of cases. However, when symptoms of hyperthyroidism are present or when compression symptoms are significant, either subtotal thyroidectomy or irradiation would appear to be strongly indicated.

Riedel's disease. As in the late stages of Hashimoto's disease, hypothyroidism is usually present in woody thyroiditis or Riedel's disease. The gland in this condition is so firm that it is readily confused with carcinoma. One important aid in differentiation is the fact that in carcinoma the basal metabolic rate is usually normal or slightly elevated, whereas in Riedel's disease it is usually below normal, particularly in the latter stages when induration is pronounced. Another point of differential value lies in the fact that if nodes are palpable alongside the thyroid, the diagnosis of carcinoma can usually be made safely, since nodes are seldom involved in Riedel's disease.

Theoretically, removal of the thyroid gland in this condition would be undesirable since it might increase the hypothyroidism. However, there is fairly strong evidence that the thyroid in Riedel's disease is exerting little or none of the function ascribed to the normal thyroid gland.

Since symptoms of compression are so common in woody thyroiditis, thyroidectomy is usually advisable. However, there is little or no justification for attempting to be radical in removing the lobes, particularly since adhesions are frequently so dense and landmarks so obscured that even subtotal resection would seem dangerous to vital structures, the laryngeal nerves in particular. Moreover, it has

been discovered that removal of the isthmus and the anterior portion of the thyroid on each side (if both sides are involved) is sufficient to eliminate the compression symptoms.

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